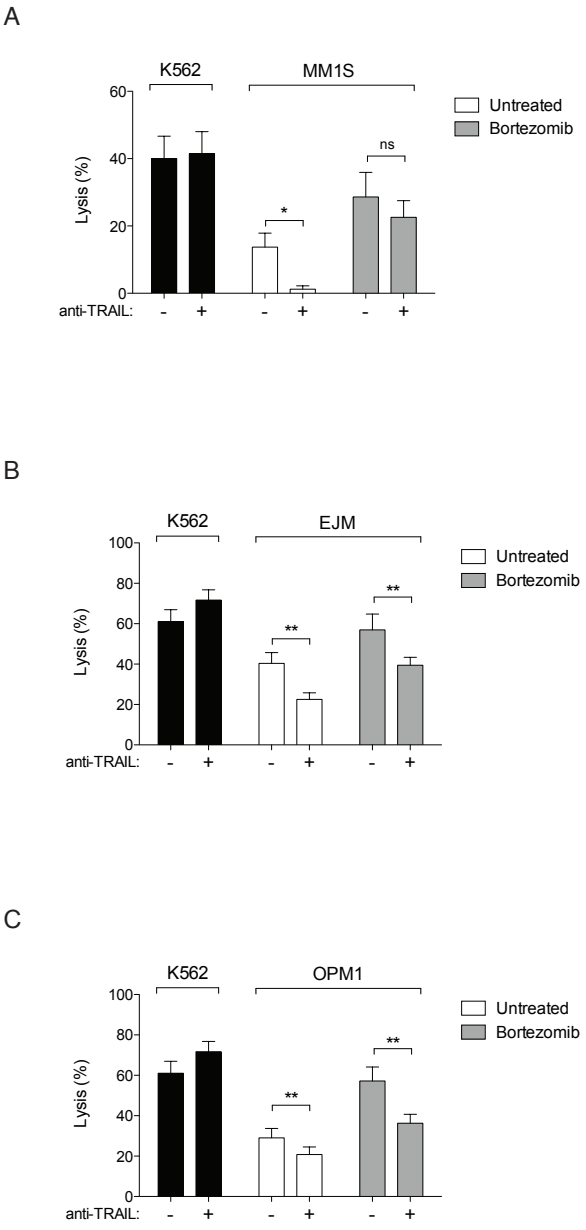
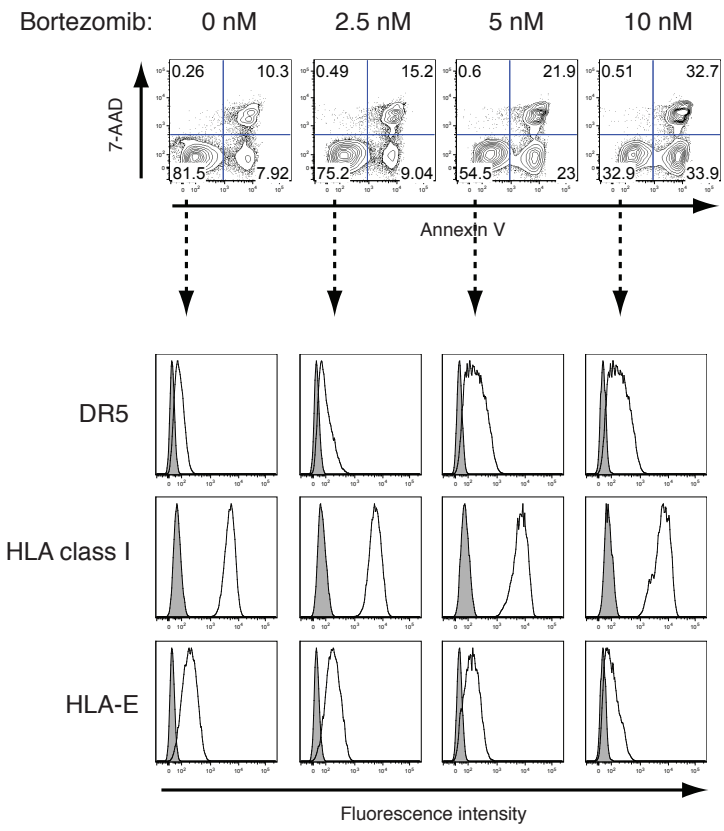
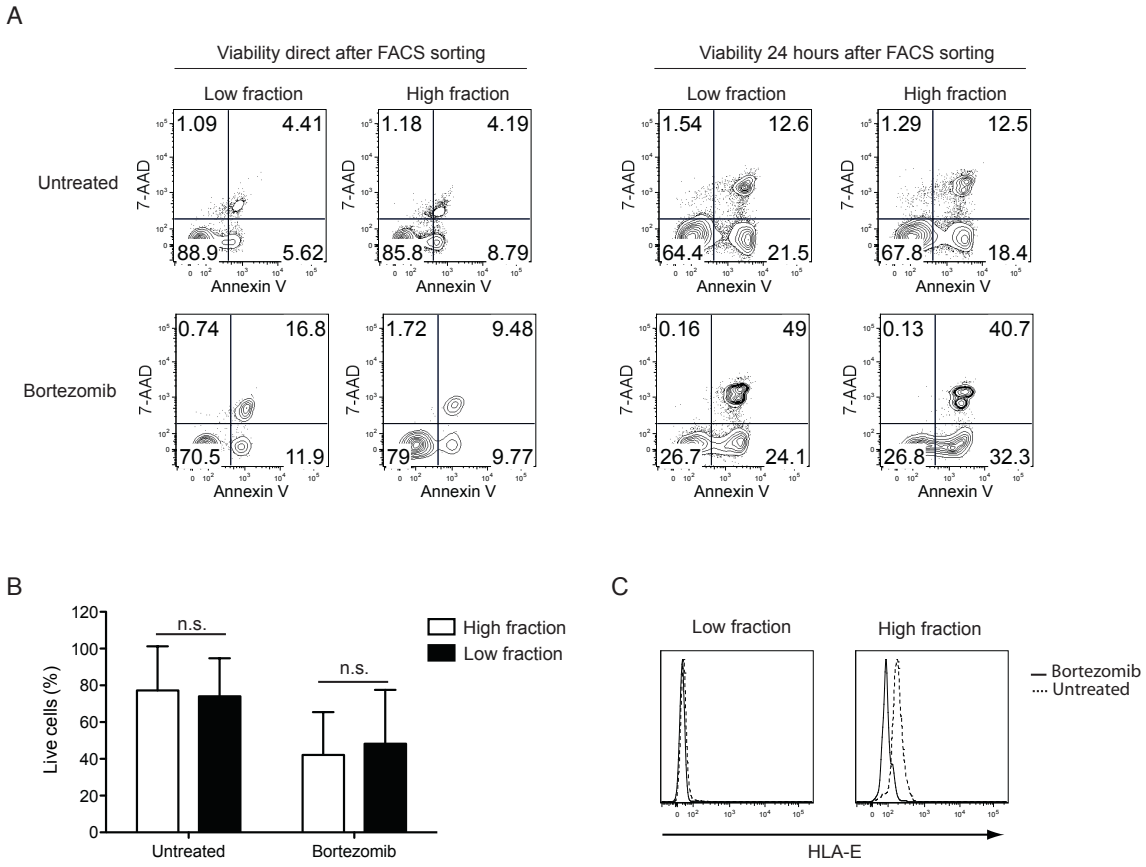
Supplemental Figures



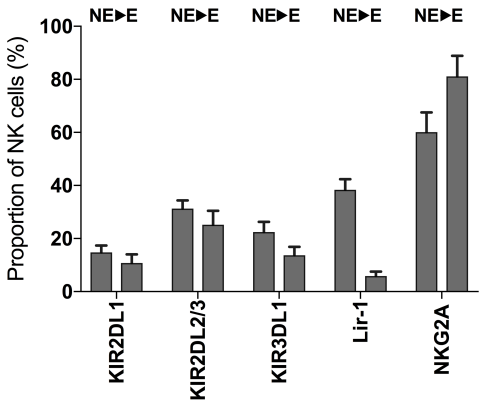
Supplemental Figure 1. TRAIL blockade of NK cells reduces their baseline cytotoxicity against MM cells but only partially reduces tumor sensitization to NK cells following bortezomib exposure. Overnight IL-2 activated NK cells were co-cultured with MM cell lines either pre-exposed (grey bars) or not (white bars) to 5 nM bortezomib for 24 hours. K562 cells (black bars) were used as a control. Lysis of (A) the EJM (n=8), (B) the MM.1S (n=6) and (C) the OPM1 (n=8) cell lines following a 4-hour co-culture with NK cells either not blocked or pre-blocked with a TRAIL antibody. *Bars*, mean. *Error bars*, standard deviation. * $p < 0.05$, ** $p < 0.01$.



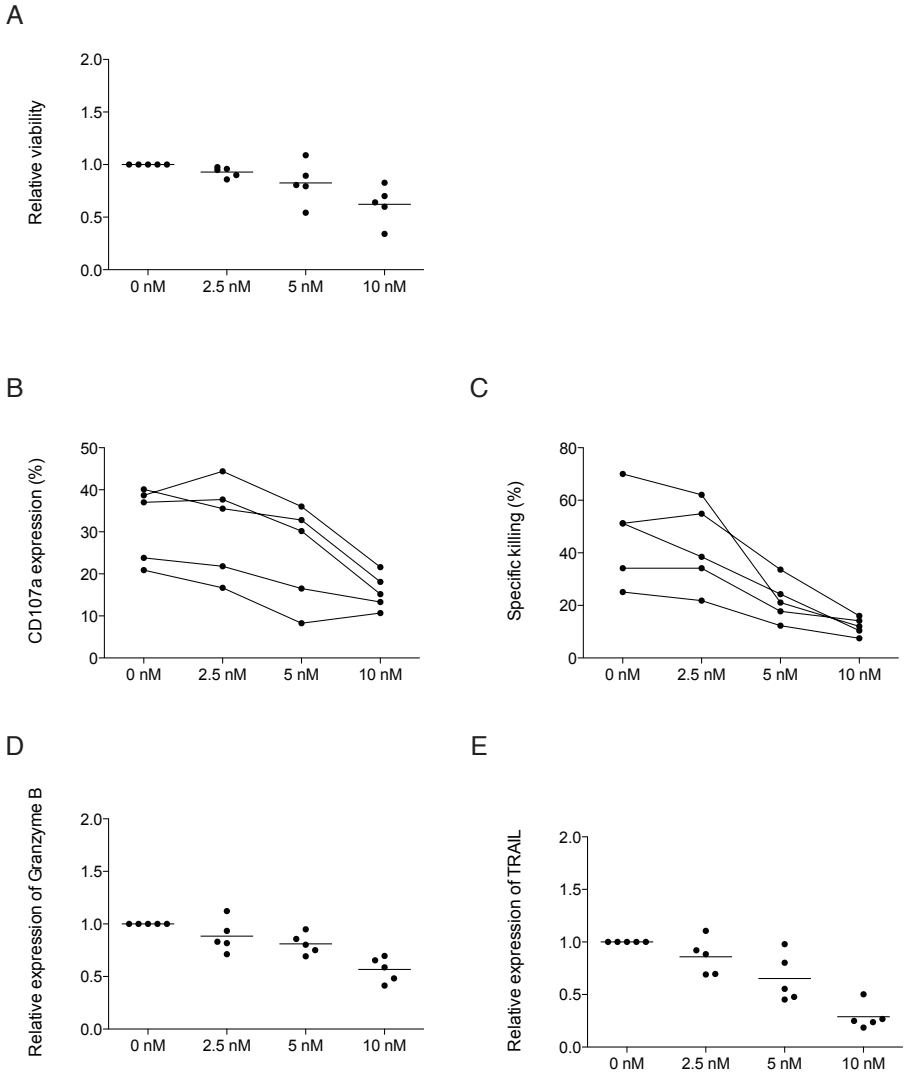
Supplemental Figure 2. Dose-dependent loss of HLA-E expression on MM cells following exposure to bortezomib. The MM cell line OPM1 was exposed to increasing doses of bortezomib for 24 hours before cell viability was measured using 7-ADD and Annexin V and DR5, HLA class I and HLA-E expression was assessed on 7-AAD$^-$/Annexin V$^-$ live cells. One representative example is shown. *Histogram lines*, molecule expression. *Tinted histogram*, isotype control.



Supplemental Figure 3. Loss of HLA-E expression on the MM cell surface following exposure to bortezomib is not a consequence of drug-induced cell death. The viability of flow cytometry-sorted bortezomib-exposed (5 nM) and unexposed HLA-E^{low} and HLA-E^{high} MM cells was measured directly or 24 hours after sorting using 7-ADD and Annexin V. (A) Representative flow cytometry plots showing the viability of MM cell directly after flow sorting (left panel) and 24 hours from flow sorting (right panel). (B) Diagram showing the cell viability of the two sorted cell fractions (HLA-E^{high}, white bars. HLA-E^{low}, black bars) for unexposed and bortezomib-exposed cells (n=3). (C) Representative examples of HLA-E expression on bortezomib-exposed and unexposed sorted MM cell fractions. *Bars*, mean. *Error bars*, standard deviation. ns, non-significant. *Histogram lines*, bortezomib-treated MM cells. *Dotted histogram*, no bortezomib MM cells.



Supplemental Figure 4. Expression of inhibitory HLA class I-binding receptors on NK cells before and after *ex vivo* expansion for 14 days. The expression of KIRs, the Lir-1 and the NKG2A receptors was assessed before (non-expanded NK cells; NE) and after 14 days of *ex vivo* expansion (expanded NK cells; NE).



Supplemental Figure 5. Viability and function of non-expanded healthy donor NK cells following exposure to bortezomib for 24 hours. The viability, function and expression of granzyme B and TRAIL was measured on non-expanded healthy donor NK cells after 24 hours of exposure to increasing concentrations of bortezomib. (A) Relative viability of bortezomib-exposed NK cells compared to unexposed NK cells. (B) Degranulation as measured by CD107a by unexposed and bortezomib-exposed NK cells following co-cultures with K562 cells. (C) Specific lysis of K562 cells by unexposed and bortezomib-exposed NK cells as measured by ^{51}Cr release assay. (D) Relative expression of granzyme B by bortezomib-exposed NK cells compared to unexposed NK cells. (E) Relative expression of TRAIL by bortezomib-exposed NK cells compared to unexposed NK cells.